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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Jacques DUMAS et al.	:	
Serial No.: 09/776,935	:	Group Art Unit: 1617
Filed: December 22, 1998	:	Examiner: MITCHELL, Gregory W.

For: INHIBITION OF p38 KINASE USING ARYL AND HETEROARYL SUBSTITUTED HETEROCYCLIC UREAS

REPLY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SIR:

In response to the Office Action mailed on December 30, 2005, please consider the remarks.

The only outstanding rejection alleges a lack of enablement for the treatment of rheumatoid arthritis with the compounds recited in the claims.

First and foremost, there is no indication that one of ordinary skill in the art would have questioned the effect of the drugs in view of the disclosure and the state of the art. See *Rasmusson v. Smithkline Beecham Co.*, 75 USPQ2d 1297 (CA FC 2005). Thus, the enablement rejection is improper.

Applicants teach that "inhibition of p38 has been shown to inhibit both cytokine production (eg., TNFα, IL-1, IL-6, IL-8) and proteolytic enzyme production (eg., MMP-1, MMP-3) *in vitro* and/or *in vivo*." See page 2 of the specification. Applicants also cite a large volume of prior art that provides the nexus between, for example, TNFα and various diseases, including rheumatoid arthritis. See pages 2-5 of the specification. Applicants teach on page 5 of the specification that "because inhibition of p38 leads to inhibition of TNFα production, p38 inhibitors will be useful in treatment of the above listed diseases," which includes rheumatoid arthritis.

Applicants bring to the attention of the Examiner that there are currently at least three FDA approved rheumatoid arthritis therapeutics whose target is TNFα, e.g., Remicade® (infliximab) of Centocor Inc.; Enbrel® (etanercept) of Immunex/Wyeth; and Humira®